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10/538,442	09/11/2006	Jean Pierre Gayral	GENOM.061NP	3808

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/538,442	GAYRAL ET AL.	
	Examiner	Art Unit	
	CYNTHIA B. WILDER	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) *1-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/6/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 11/6/2008 is acknowledged and has been entered. Claims 15, 17, 30, 32, 46 have been amended. Claims 1-46 are pending. Claims 1-14 are withdrawn from consideration as being drawn to a non-elected invention. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejections

3. The prior art rejection under 35 USC 102(b) as being anticipated by Berg et al is withdrawn in view of the new ground(s) of rejections necessitated by Applicant's amendment of the claims. The prior art rejection under 35 USC 103(a) as being unpatentable over Berg et al in view of Ke et al and Kruske et al is withdrawn in view of the new grounds of rejections necessitated by Applicant's amendment of the claims. The prior art rejection under 35 USC 103(a) as being unpatentable over Berg et al in view of Picard et al and Bergeron et al is withdrawn in view of the new grounds of rejections necessitated by Applicant's amendment of the claims.

New Ground(s) of Rejections

THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY AAPLICANT'S AMENDMENT OF THE CLAIMS:

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 15-18, 23-29, 32-34 and 39-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berg et al (WO 02/18635, March 2002) in view of Kolk et al (Journal of Clinical Microbiology, vol. 32, No. 5, pages 1354-1356, May 1994) .

Regarding claims 15 and 32, Berg et al teach a method for verifying the efficiency of sample preparation of test sample nucleic acids and the performance of nucleic acid amplification and detection practiced on a test sample after its preparation, said method comprising: providing a an internal control reagent comprising non-viable viral particles, said internal control reagent having at least one internal control (IC) nucleic acid sequence therein, wherein said internal control reagent is an internal

control for the release, amplification and detection of a nucleic acid from said test sample; (ii) adding said internal control reagent into said test sample; (iii) submitting said test sample with said added internal control reagent to a sample preparation procedure in order to release, both said nucleic acid from said test sample and said IC nucleic acid target sequence from said internal control reagent added reagent ; and (iv) submitting a product from said sample preparation procedure to amplification and detection for the amplification and detection of both said IC nucleic acid target sequence and said nucleic acid of the test sample nucleic acids, wherein detection of said IC nucleic acid target sequence is indicative of both efficient sample preparation and performance of nucleic acid amplification (page 4-9, lines 1-19; lines 10, lines 6-21 and 31-37). Berg et al teach that the sample may be derived from cultured cells, bacteria or viral particles *(in vitro* source) or from human; plant or animal sources (*in vivo* sources) (page 31). Berg et al further teach that the target nucleic acid include cells, derived from multicellular organism or unicellular organisms as well as viruses and bacteriophages (page 19, lines 33-36).

While Berg et al prefers using non-viable viral particles as the internal control, Berg et al teaches that internal control can have a variety of forms. Berg et al recognizes viable cells can be used as an internal control. Berg et al cites Kolk et al to support this conclusion (page 4). Berg et al teaches an important feature of any internal control sequence for use in nucleic acid based assays is that it can be distinguishable from the target sequence in the subsequent analysis or detection of the nucleic acid molecules produced.

Kolk et al teach a method for determining the efficacy and quantification of a target molecule (bacterial) in a sample, wherein said method comprises the use of an internal control, wherein said internal control genetically engineered viable bacterial cells (see pages 1355 and 1356). Kolk et al teach that the genetically engineered bacterial cells can be used as an effective internal control, which allows monitoring of the efficacy of DNA extraction and the presence of PCR-inhibiting substances (page 1356, first paragraph of column 1).

Thus, it would have been obvious to a person of ordinary skill in the art at the time of the claimed invention to use a viable internal control cell or non-viable internal control cell as taught by Berg et al and Kolk et al in a method for determining a target molecule since a person with ordinary skill has good reason to pursue the known options within his or her technical grasp. In turn, because the use of a viable or non-viable internal control effectively allows the monitoring of the efficacy of DNA in a target molecule as taught by the prior art. The ordinary artisan could predictably expect a reasonable expectation of success using a viable cell or non-viable cell as an internal control in the method as claimed based on the teachings of Berg et al in view of Kolk et al. The combined teachings of Berg et al and Kolk et al are deemed *prima facie* obvious in the absence of secondary consideration.

Regarding claims 16, Berg et al teach further comprising (v) comparing the amplification and/or detection performed in iv) to the amplification and detection performed with a control reaction to evaluate the efficiency of the sample preparation

and the performance of the nucleic acid amplification and detection practiced on said test sample and reagent (page 37, lines 10-29).

Regarding claims 17 and 33, Berg et al teach wherein said sample preparation procedure comprises purifying cells and non-viable viral particles prior to lysis (page 35, lines 1-3).

Regarding claims 18 and 34, Berg et al teach wherein said cells are selected from bacteria (see Examples at pages 41-50, e.g., Example 2 which teaches *Chlamydia trachomatis).*

Regarding claims 23-24 and 39-40, Berg et al teach wherein said IC target nucleic acid target sequence is on such as a plasmid (page 4, lines 3-4).

Regarding claims 25 and 41, Berg et al teach wherein said nucleic acid amplification method is PCR (page 8, line 35 to page 9, line 1-4).

Regarding claims 26 and 42, Berg et al teach wherein said IC target nucleic acid target sequence is nucleic acid sequence of clinical, environmental, alimentary or human origin (page 31, lines 31-37 to page 32, lines 1-16).

Regarding claims 27 and 43, Berg et al teach wherein said IC target nucleic acid target sequence is a nucleic acid sequence of microbial origin (see Examples).

Regarding claims 28-29 and 44-45, Berg et al teach wherein the said test sample is a sample of clinical origin and wherein said test sample comprises a vaginal swab (see page Examples and see also pages 31 and 32). Therefore, Berg et al meet the limitations of the claims recited above.

Response to Arguments

7. Applicant traverses the citation of Berg et al on the following grounds: Applicant state that Berg et al does not meet the limitation of the claims because the claimed subject matter is currently directed toward methods that use viable internal control reagents. Applicant states that the specification in examples 1 and 2 have demonstrated that the viable reagents, E. Coli cells and Bacillus globigii spores, could serve as effective internal control. Applicant states that in contrast to Applicant's teaching relating to the use of viable internal control reagents, Berg describes the use of non-viable particles containing an internal control nucleic acid and cited the advantages for using viable internal control cells. With regards to target nucleic acid, Applicant states that in the context of Applicants' claims refer only to IC target nucleic acid. Applicant states that Berg et al streses that IC nucleic acids are non-viable, as such the target nucleic acid cannot include viable organisms as asserted by the Examiner.

8. All of the arguments have been thoroughly reviewed and considered. However, they are not found persuasive for the reasons that follow: In response to Applicant's arguments that the claims of the instant invention are only limited to viable internal control, the Examiner respectfully disagree as nowhere in the instant specification do the specification define that the various "cells" as claimed for the internal control are "viable". Likewise, the claims as currently written are not limited to only "viable cells". Additionally, there is no definition in the art which would inherently imply that because the term "cell" is used that it automatically implies only "viability". It is noted that the courts have established that during patent examination the pending claims must be

interpreted as broadly as their terms reasonably allow (*In re Zletz, 893 F.2d 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).* In this case, the term "cell" can broadly be interpreted as encompassing "viable" or "non-viable" elements. While the Examiner agrees that Berg et al prefers the use of non-viable viral particles. Berg et al expressly teach that internal control sequences can have a variety of forms, including that of viable bacterial cells as evidence by Kolk et al (see rejection above). MPEP states that "[A] known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994)". In this case, while Berg et al teaches that non-viable internal control sequences are advantageous, it does not change the fact that Berg recognizes that viable cells can be used for the same purpose and cites Kolk et al which provides evidence of viable bacterial cells being effectively used to monitor the efficacy of a target molecule in a sample. Hence, the same purpose as argued by Applicant. In response to Applicant's arguments concerning the advantages of the instant invention (using viable cells), this argument is not persuasive, because the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). In this case, as noted earlier, Berg recognizes that viable cells can be use as an internal control reagent. Kolk provides sufficient evidence to support this conclusion. Therefore, it would be obvious to

the ordinary artisan that one could use either types of internal control reagents based on the practitioner's desired results.

With regards to Applicant's arguments concerning the target nucleic acids, it is noted that Applicant claims are not limited in the manner argued by Applicant. There is nothing in the claims which would suggest that "only IC target nucleic acid" are used. It is again noted that the courts have established that during patent examination the pending claims must be interpreted as broadly as their terms reasonably allow (*In re Zletz, 893 F.2d 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).* In this case, the claims recite open language in the recitation of "comprising" which allows the inclusion of unrecited or appreciated elements. Further, Applicant is additionally reminded that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, it is noted that the claims do not by any means exclude "non-viable target molecule" or "non-viable internal control nucleic acids". Applicant's arguments are not sufficient to remove the prior art teachings of Berg et al.

9. Claims 19-21, 31, 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berg et al in view of Kolk et al as previously applied above in view of Ke et al (citation made of record in prior Office action) and Kruske et al (citation made of record in the prior Office action).

Berg et al in view of Kolk et al teach a teach a method for verifying the efficiency of sample preparations of test sample nucleic acids by providing an internal control reagent, adding the internal control reagent into said test sample, submitting said test sample with said added internal control reagent to a sample preparation procedure in order to release both said nucleic acid from said test sample and said IC nucleic acid target sequence from said internal control reagent and submitting a product from said sample preparation procedure to amplification and detection of both said IC nucleic acid and target sequence. Berg et al and Kolk et al additionally teach wherein said internal control reagent comprises cells from a bacterial origin.

With regards to claims 19-21, 31 and 35-38, Berg et al in view of Kolk et al do not teach wherein said cells are *E. coli* cells or *Bacillus globigii* spores. However, the desired selection of cells for use in the method is based on conventional nucleic acid manipulation of reagents and methodologies, as well as well as routine optimization of reaction components, concentrations, and parameters. Clearly such conventional and trivial modification and optimizations do not contribute towards patentability.

For example, Ke et al teach a method of providing an internal control reagent for verification of reaction conditions, wherein said internal control reagent comprises cells derived from *E. coli* (page 325, col. 2, "construction of the internal control" and Table 1). Ke also teaches wherein the internal control reagent comprises cells derived from bacterial spores such as *bacillus anthracis* (Table 1).

Kruske et al teach a method similar to that of Ke et al wherein an internal control reagent is provided, said internal control reagent comprises cells derived from *Bacillus*

globigii endospores, said cells isolated from an environmental sample (page 2463 and 2471).

Thus, one of ordinary skill in the art would have been motivated to modify the primary references in the manner of the claims to achieve the expected benefits, optimizations and/or expanded applications. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods using different cell types isolated from different sources.

10. Claims 30 and 46 rejected under 35 U.S.C. 103(a) as being unpatentable over Berg et al in view of Kolk et alas previously applied above, in view of Picard et al and Bergeron (citation made of record in prior office action). Regarding claims 30 and 46, Berg et al in view of Kolk et al teach a teach a method for verifying the efficiency of sample preparations of test sample nucleic acids by providing an internal control reagent, adding the internal control reagent into said test sample, submitting said test sample with said added internal control reagent to a sample preparation procedure in order to release both said nucleic acid from said test sample and said IC nucleic acid target sequence from said internal control reagent and submitting a product from said sample preparation procedure to amplification and detection of both said IC nucleic acid and target sequence. Berg et al and Kolk et al additionally teach wherein said internal control reagent comprises cells from a bacterial origin.

Berg et al in view of Kolk et al do not teach wherein the sample preparation procedure comprises steps of nucleic acid extraction and elimination, neutralization and inactivation of nucleic acid testing (NAT) inhibitors.

Picard et al and Bergeron teach a method comprising providing a reagent comprising a cell comprising bacterial cells comprising at least one nucleic acid sequence serving as an internal control target sample preparation; adding said internal control into said test sample, submitting a released, nucleic acid to amplification or detection and further comparing the amplification and/or detection with control reactions to evaluate the efficiency of the preparation (see section 2.2 and 2.5-2.5.3.).

Picard and Bergeron further teach wherein the sample preparation comprises concentrating and purifying cells or viral particles, lysis of cells, nucleic acid extraction, inactivation, elimination or neutralization of NAT inhibitors and nucleic acid concentration or purification (see section 2.2. and 2.5 to 2.5.2). Picard and Bergeron teach that the above steps provide optimum results in sample preparation versus prior methods for preparing a nucleic acid sample from a microbial cell (section 2.2). Picard and Bergeron teaches that internal controls are important and that they are integrated into the NAT assay to verify the efficiency of each amplification and/or detection reaction (see 2.5.2 and section 3, "Conclusion and perspectives").

One of ordinary skill in the art at the time of the claimed invention would have been motivated to incorporate steps of preparing a sample as taught by Picard and Bergeron wherein a NAT assay is used for verifying the efficiency of an amplification and/or detection reaction as taught by Berg et al in view of Kolk et al for the benefit of

obtaining optimum results when preparing a nucleic acid sample from a microbial cell a suggested by Picard and Bergeron. The instant invention is *prima facie* obvious over the combined teachings of Berg et al and Kolk et al in view of Picard and Bergeron.

Response to Arguments

11. Applicant traverses these rejection on the same grounds discussed above for Berg et al. Applicant states that the secondary references do not cure the deficiencies of the Berg et al prior art.

12. All of the arguments have been thoroughly reviewed and considered but are maintained for the same reasons discussed above at # 8.

Conclusion

13. No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

/CBW/

/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637